Name and degrees of Principal Investigator: Jane E Gallagher Ph.D
Department: Human Studies Division US EPA Mailing address/CB #: 7315
UNC-CH PID: NA Pager: NA
Phone #: 919-966-0638 Fax #: 919-966-0655 Email Address: gallagher.jane@epa.gov

For trainee-led projects: __ undergraduate __ graduate __ postdoc __ resident __ other
Name of faculty advisor:
Department: Mailing address/CB #:
Phone Fax #:

Name, phone number, email address of project manager or coordinator, if any:

List **all other project personnel** including co-investigators, and anyone else who has contact with subjects or identifiable data from subjects: Ed Hudgens, Lucas Neas, Ann Williams, Gina Andrews, Mary Johnson, Ron Williams, Danielle Lobdell (US EPA), Christine Johnson and Ganesa Wegienka (Henry Ford Health System Detroit Michigan-(HFHS).

Name of funding source or sponsor:
__ not funded X Federal __ State __ industry __ foundation __ UNC-CH
__ other (specify): **Sponsor or award number**: US Environmental Protection Agency

Part A.4. Questions Common to All Studies

For all questions, if the study involves only secondary data analysis, focus on your proposed design, methods and procedures, and not those of the original study that produced the data you plan to use.

A.4.1. **Brief Summary**. Provide a *brief* non-technical description of the study, which will be used for internal and external communications regarding this research. Include purpose, methods, and participants. Typical summaries are 50-100 words.

Asthma is the most common chronic disease of childhood. The US Environmental Protection Agency (EPA) is interested in the interplay of environmental and genetic factors on the development and exacerbation of asthma. The proposed Mechanistic Indicators of Childhood Asthma (MICA) study uses markers of environmental exposure and health effects as well as molecular biology, chemistry, and gene technologies to identify factors that affect individual susceptibility. This information will be used to analyze, characterize, and possibly quantify combined risk factors that relate to asthma severity from multiple agents/stressors (see Fact Sheet).

MICA is a companion study to the previously approved (UNC Biomedical IRB 05-EPA-144) Detroit Children's Health Study (DCHS), a study evaluating the impact of early life exposures to mobile source emissions among children. Previously approved DCHS study materials informed the parents/guardians of participants in DCHS that they might be contacted for participation in MICA without providing any specific details of the MICA study. In the summer and fall of 2006, a selected cohort of up to 1,400 children from the DCHS questionnaire cohort with parental consent will be asked to perform a routine lung function examination at a Henry Ford Health System clinic. The examination will consist of breathing tests that involve repeated steady blows into a device that measures air flow rates and lung volumes. A second breathing test will measure exhaled nitric oxide.

MICA provides a biomarker component to the companion DCHS study. MICA will enroll 200 (100 asthmatic and 100 non-asthmatic) children aged 9-12 years from among the 1,400 children participating in the clinical portion of DCHS. MICA investigates biomarkers of dose, effect and susceptibility in a subset of asthmatic and healthy DCHS participants (aged 9-12 years); MICA will conduct identical DCHS breathing tests, but requires blood, urine, fingernail and or toenail clipping collection, and a simple odor identification test. A limited number of adult guardians of the participants will employ passive air monitoring monitors outside their home and in their children's bedroom in order to provide context to their children's biological measures of exposure, dose, effect and susceptibility (Attachment 1).

A.4.2. **Purpose and Rationale.**

RNA technology has been previously used to identify gene(s) associated with disease states, including asthma, but the studies are few and limited to adults. Previous research indicates that asthma status is readily distinguished based on the occurrence of strong gene expression signatures in nasal epithelial cell samples. A primary focus of MICA is to identify gene expression signatures in blood RNA that reflect asthma-related processes. Gene expression profiles from asthmatic and non-asthmatic children will be viewed in context of putative "at risk" genes delineated in attachment 1; Markers of exposure effect and susceptibility. MICA is a clinical examination of the associations between environmental exposures and health outcomes and interrelationships between exposure dose effects and susceptibility related to asthma/allergy outcomes. The primary objectives of MICA are as follows:

- Evaluate relationships in asthmatic and non-asthmatic children (ages 9-12) from the DCHS participants by comparing exposures, internal dose and effect markers in the context of gene expression profiles from RNA isolated from blood samples.
- Elucidate the gene:gene, genotype:phenotype, and gene:environment relationships.

Primary research questions that will be answered are as follows:

- Do levels of blood and urinary chemical metabolites and/or aeroallergens have an independent or combined role in increasing/decreasing gene expression in cells isolated from blood?
- What environmental exposures and genetic polymorphisms are predictive of allergen-specific IgE antibody test and other inflammatory biomarkers of exposure and effect?
- Are human biomarkers of exposure, early effect, and gene expression associated with home measurements of volatile organic carbons (VOCs), polycylic aromatic hydrocarbons (PAHs), nitrogen dioxide (NO_2), and metals in monitor and model-based estimates of neighborhood differences in exposure?

A.4.3. Subjects. *You should describe the subject population even if your study does not involve direct interaction (e.g., existing records).* Specify number, gender, ethnicity, race, and age. Specify whether subjects are healthy volunteers or patients. If patients, specify any relevant disease or condition and indicate how potential subjects will be identified.

Per the DCHS approved EPA IRB (EPA-05-144), in the spring of 2006, the Henry Ford Health System will identify two study populations from existing clinical records: (a) 6,000 children aged 7 to 12 years who constitute a random sample of their client population. (a) 200 children

aged 9 to 12 years with a prior clinical history of asthma. The Henry Ford Health System will handle the mail distribution of questionnaire packets to the parents/guardians of these 6,000 selected children. In the summer and fall of 2006, the Henry Ford Health System will contact the parents/guardians who complete the DCHS questionnaire in an attempt to recruit up to 1,400 children for routine measurements of exhaled breath and lung function. From this cohort the Henry Ford Health System will identify physician diagnosed asthmatic (100) and non-asthmatic (100) children. The selection will be based on asthma emergency department visits and/or medication dispensing events.

A.4.4. **Inclusion/exclusion criteria.** List required characteristics of potential subjects, and those that preclude enrollment or involvement of subjects or their data. Justify exclusion of any group, especially by criteria based on gender, ethnicity, race, or age. If pregnant women are excluded, or if women who become pregnant are withdrawn, specific justification must be provided.

All children aged 9 to 12 years who returned DCHS questionnaires who reside in the communities of Detroit, Dearborn, Highland Park, or Hamtramck and who are served by the Henry Ford Health System will be eligible for selection into the MICA study. Subjects will be recruited without regard to sex or ethnicity. Due to the diverse population of the Detroit metropolitan area, a short English-language questionnaire will be administered at the clinic to obtain recent exposure and dietary data (questionnaire). Due to issues of reliable parental informed consent and the coaching during the clinical measurements, parents/guardians who are not capable of providing informed consent in English will be excluded from the study.

Any child with a history of respiratory illness in the last two weeks, or who have ever smoked ten or more cigarettes, or who has been a carrier of a communicable disease will be excluded from the pulmonary function examination. No child will be excluded from participating in the pulmonary examinations due to any chronic, non-infectious respiratory problems or environmental exposures. However, to control for potential confounding by rare conditions with strong pulmonary effects, the analysis of the environmental associations will exclude children with a history of cystic fibrosis, chest operation, heart conditions, or who received oxygen for more than two weeks after birth or at home. Children with any of these conditions, with acute respiratory illnesses, or active smokers will be excluded from the pulmonary exams.

A.4.5. **Full description of the study design, methods and procedures.** Describe the research study. Discuss the study design; study procedures; sequential description of what subjects will be asked to do; assignment of subjects to various arms of the study if applicable; doses;; how data are to be collected (questionnaire, interview, focus group or specific procedure such as physical examination, venipuncture, etc.). Include information on who will collect data, who will conduct procedures or measurements. Indicate the number and duration of contacts with each subject; outcome measurements; and follow-up procedures. If the study involves medical treatment, distinguish standard care procedures from those that are research. If the study is a clinical trial involving patients as subjects and use of placebo control is involved, provide justification for the use of placebo controls.

Study participants will include 100 asthmatic and 100 non asthmatic children selected from DCHS participants. The families will be selected and contacted by the Henry Ford Health System (HFHS). The recruitment contact will be conducted by mail and by telephone (see telephone script), and may involve repeated contacts in order to schedule the clinical visit. Informed parental consent and the child's assent will be obtained at the start of the clinic visit.

An educational Power Point presentation with voice-over animation and an overview of the assessments that will occur in each of the stations as shown in the attached Power Point computer visual. The presentation will precede the consent and assent process. The clinical visit will include lung volume and rate and expired NO_2 measurements, a blood draw, a urine sample and fingernail/toenail collections. The DCHS approved protocol (EPA-05-144) provides a 6,000-family questionnaire cohort selected by the Henry Ford Health System. EPA will select a 1400-family cohort from those families returning the questionnaire for a clinic visit that will entail two breathing tests (spirometry and expired nitric oxide). MICA is a companion study to the DCHS protocol that will add a biomarker component. A description of clinical procedures that will take place the day of the MICA clinical visit follows:

- **Home monitoring**: 50% of MICA participants will be selected and pending their interest will be shipped an indoor and outdoor home passive monitoring kit. Half of the participants who conduct air monitoring will receive a sampling kit for NO_2, and volatile organic compounds (VOC). The other half of will receive a kit for sampling NO_2, PAH, and naphthalene. The kit will be returned at the prescheduled clinic visit. Participants who forget to bring the kits or their vacuum dust samples with them to their clinic appointment will be given the option of dropping off at a later date. They will be provided with drop off information (see attachment A1 Some MICA participants who express interest may be called back and notified that we will not be able to enroll them due to circumstances such as lack of supplies, scheduling logistics, etc. (see attachment A2).

  To ensure meaningful analysis of air sampling data, duplicate samplers will be sent to some air monitoring households. To reduce overall burden to the participant, no household will receive more than one additional sampler, and the extra sampler will be identical to one of the other samplers in their kit. Each household will receive a customized sampling kit with instructions that address the quantity and type of samplers in their sampling kit. There are 12 slightly different versions of the instructions (see attachments A, B, and C).

  The air monitoring strategy may undergo minor changes to provide additional clarity and address challenges encountered by participants in carrying out the air sampling. These changes may include: updated pictures and photos, minor editorial changes, additions, and deletions in formatting and language, additional technical language to address challenges or obstacles encountered when the samplers are deployed in the field, changes in color-coding scheme, sampling duration, time of deployment, and temperature collection, etc.

- **Presentation**: Computer-based visual aid with audio (6 minutes) describing asthma, asthma attacks and typical asthma triggers. The presentation will also show various examination stations that the child will go through as part of the clinic visit.
- **Questionnaire**: A brief questionnaire will collect the child's recent medical history, including medications taken, smoking history, short, time-activity questions, and a summary of the child's daily diet (questionnaire).
- **Body size**: The child will be asked to stand for height and weight measurement.
- **Vital Signs**: A trained technician will measure the child's blood pressure and oxygen saturation.
- **Blood collection**: A trained phlebotomist will collect 50ml (about 10 teaspoons) of blood from the child. The blood collection entails a risk of mild discomfort with the infrequent possibility of blood hematoma formation. There is also a small risk of infection. Some

participants may feel faint after the blood draw. A Henry Ford Health System physician will be available during all clinical procedures. No more than two attempts to draw blood will be made.

- **Urine Collection**: Urine will be collected in a container fitted to the top of a toilet lid. Medical staff personnel will retrieve the sample and pour the urine into a specimen cup.
- **Breathing capacity:** After a careful explanation of the procedure and a demonstration by a respiratory technician, the child will be asked to take the deepest possible breath and then immediately exhale as quickly as possible until she/he can exhale no more air. The breathing vital capacity will be repeated 3 to 8 times. A new clean filter/mouthpiece will be used for each participant.
- **Exhaled Nitric Oxide** After a careful explanation of the procedure and a demonstration by a respiratory technician, the child will be asked to exhale a volume breath. Each child will use a clean filter mouthpiece. The exhaled nitric oxide test will be repeated 3-5 times for accuracy.
- **Smell test**: The child will be ask to perform an odor identification test involving scratching and sniffing little paper bubbles containing various smells. The child will try to identify 10 smells by marking one of four choices for each smell.
- **Fingernail/toenail clippings** The child will be asked to clip 10 fingernails or substitute toenails if they unable or unwilling to provide fingernails. The parent or guardian can assist the child. If both fingernail and toenail clippings are needed, the child will separate them into separate Ziplock bags. The child can take the clippers home.

A.4.6. **Benefits to subjects and/or society.** Describe any potential for direct benefit to individual subjects, as well as the benefit to society based on scientific knowledge to be gained; these should be clearly distinguished. Consider the nature, magnitude, and likelihood of any direct benefit to subjects. If there is no direct benefit to the individual subject, say so here and in the consent form (if there is a consent form). Do not list monetary payment or other compensation as a benefit.

Attempts to reduce disease incidence are hampered by incomplete understanding of the contribution of multiple environmental and genetic factors on the pathogenesis of asthma. Understanding the components that impact asthma should improve early prediction, cost-effective testing and diagnosis of disease. Gene expression analysis, bioinformatics, and computational toxicology will provide more meaningful data for risk assessment as compared to studies that focus on discrete biological events in a source-to-outcome paradigm. The study will measure the interaction among multiple environmental exposures, personal characteristics, and internal dose markers, resulting in a better understanding of the underlying causes of disease. This understanding may lead to a more cost-effective preventive measure against the environmental components of allergic disease. There is no direct benefit to the subjects. However, blood lead levels that exceed recommended blood levels will be reported back to the participant in accordance with Henry Ford Health System policy. An allergy report will be provided to any participant exhibiting elevated levels of IgE-specific antibodies to common food or air-borne allergens. Clinical blood chemistry results will also be sent back to the participants to include blood cholesterol levels. Blood cell number and type will also be reported back as well as height weight and blood pressure measurements.

A.4.7. **Full description of risks and measures to minimize risks.** Include risk of psychosocial harm (e.g., emotional distress, embarrassment, breach of confidentiality), applicable, and risk of pain and physical injury. Describe what will be done to minimize these risks. Describe procedures for follow-up, when necessary, such as when subjects are found to be in need of medical or psychological referral.

All research includes some amount of risk/discomfort. Some risks may be unforeseeable. In this study, several measures have been taken to minimize risk to the volunteer subjects. First the professional skills and facilities of the Henry Ford Health Medical Center will be available for consultation and emergency or follow-up treatment. Second an educational module will be given as part of the assent/consent procedure to provide the child with an understanding of asthma and related triggers and will provide information as to why researchers are collecting the various biological samples. Finally information regarding what will happen in each of the clinical stations will minimize anxiety of both adult and child as shown in the attached Power Point presentation.

Data from breathing tests and other clinical measures will be recorded appropriately i.e. as charts, data sheets, electronic databases, strip chart recorders. All information provided by the subject to the investigators and all information that is collected about the subject by the investigators' will be kept confidential to the extent that is provided by law. Subject identifiers will be stripped from all data record and kept in a secure locked cabinets accessed only by the principal investigator and co-investigators. Analytic data will be identified only through subject ID numbers. Computer data filed containing de-identified data will be password protected and stored on secure drives. Subjects names will not be used in any publication. Access to the record of this study will be provided by the identifying number only and given only to those individuals associated with the study who require access to the data to perform their duties. All such individuals will be bound by this confidentiality agreement.

A.4.8. Data **analysis.** Tell how the qualitative and/or quantitative data will be analyzed. Explain how the sample size is sufficient to achieve the study aims. This might include a formal power calculation or explanation of why a small sample is sufficient (e.g., qualitative research, pilot studies).

Sample Size /Power calculations

MICA allows for the comparison of multiple markers of exposure, effects, and susceptibility in asthmatic and non asthmatic children. Sample size and power calculations are dependent on genetic effects, environmental effects and gene:environment interactions. A major aim of the study is to assess whether gene expression data will assist in better deciphering gene:environment interactions and help to identify factors that act singularly or together to affect individual susceptibility. To date, very few studies have examined the utility of gene expression data in these regards. In consideration of sample size and power calculations studies show that gene expression data over time is consistent and varies less within than between individuals, an important criteria when validating the utility of a marker. Gene expression data can decipher differences in exposed versus non-exposed individuals (e.g. smokers and non-smokers) and diseased versus healthy individuals, including mild-moderate and severe asthmatics. The results from these studies suggest that statistical power for a sample size of 100 asthmatic and non-asthmatic individuals is likely to be sufficient to reliably detect genes that distinguish between these two groups. Table 1 shows power calculations for assumed varied group proportions differences. When there are multiple genes that affect asthma, the probability that any one of those genes will be detected greater than the nominal power of 0.8 for one gene.

Table 1. Estimated power to detect any differences between asthmatics and non-asthmatics

Assumptions:	Two-sided test 0.05 Test significance level 100 subjects per group. Group1 (asthmatic) group 2 (non-asthmatic)			
A). Assume One gene or combination of genes (or other set of combined markers) that are twice as common in asthmatics relative to non asthmatics.				
group 1 proportion	0.30	0.36	0.40	0.50
group 2 proportion	0.15	0.18	0.20	0.25
Power	66	77	84	94
B Assumes One gene or combination of genes (or other set of combined markers) that are 1.5 times as common asthmatics relative to non-asthmatics.				
group 1 proportion	0.45	0.60	0.69	0.75
group 2 proportion	0.30	0.40	0.46	0.50
Power	53	77	88	94
C Assumes One gene or combination of genes (or other set of combined markers) will rarely be present in the general population (group 2) relative to the asthmatic population (group 1).				
group 1 proportion	0.50	0.40	0.30	0.20
group 2 proportion	0.10	0.10	0.05	0.05
Power	99	99	99	85

Statistical Analysis

Individual and summed indoor exposure measurements (naphthalene, phenanthrene, several volatile organic compounds, NO_2, Polycyclic aromatic hydrocarbon and metals, and dust allergens and blood specific IgE antibodies will be used in regression analyses of biomarkers of exposure: urinary levels of analytes (napthols,1-hydroxypyrene, urinary mutagenicity); levels of blood markers (cell surface markers, Reactive oxygen species, cytokines, c-reactive protein); and serum allergen- specific IgE antibody tests, lung function, expired nitric oxide levels; and biomarkers of susceptibility including polymorphism in 6 genes (Table 1: markers of exposure effect and susceptibility; attachment 1). Dust aeroallergens and mold values (ng/g)dust will be weighted as the sum of allergens and will be viewed in the context of specific blood IgE antibodies determined by serum testing and in relation to lung function measurements. Combined exposure indexes from measurements of indoor allergens and indoor and outdoor PM related pollutants will be analyzed in context of internal dose, effect and susceptibility markers (table 1).

Multivariate linear regression models will be used to test the association of exposures with internal measures of exposure, effect and susceptibility after adjustment for confounding and effect modifying exposures. Curves will be generated for non-asthmatics and asthmatics and tested for statistical differences between them. Separate curves will be drawn based on differences in individual polymorphisms, allergenicity and combined indexes for exposure and effects markers.

The computational analysis needed to ultimately integrate the data across the sources to outcome paradigm is enormous, requiring data access and management data mining, data interchange and data reduction. With direction from the Computational Toxicology Center at the US EPA, the EPA National Center for Environmental Assessment recently awarded a EPA STAR grant to the

UNC (Chapel Hill). It is expected that this cooperative agreement, will allow for the analysis of the MICA data base (particularly the gene expression data in the context of the exposure and biomarkers data). The data will should be of benefit to this group as they develop and validate multiple bioinformatic approaches to, e.g. elucidate complex biological networks and pathways relevant to asthma/allergies.

A.4.9. Will **you collect or receive any of the following identifiers?** Does not apply to consent forms.

__ No X Yes *If yes, check all that apply*:

a. **X**_ Names
b. **X** Telephone numbers
c. **X** Any elements of dates (other than year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death. For ages over 89: all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 and older
d. __**X** Any geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code and their equivalent geocodes, except for the initial three digits of a zip code
e. **No** Fax numbers
f. **No** Electronic mail addresses
g. **No** Social security numbers
h. **No** Medical record numbers
i. __ Health plan beneficiary numbers
j. __ Account numbers
k. __ Certificate/license numbers
l. __ Vehicle identifiers and serial numbers (VIN), including license plate numbers
m. __ Device identifiers and serial numbers (e.g., implanted medical device)
n. __ Web universal resource locators (URLs)
o. __ Internet protocol (IP) address numbers
p. __ Biometric identifiers, including finger and voice prints
q. __ Full face photographic images and any comparable images
r. __ Any other unique identifying number, characteristic or code, other than dummy identifiers that are not derived from actual identifiers and for which the re-identification key is maintained by the health care provider and not disclosed to the researcher

A.4.10. **Confidentiality of the data**. Describe procedures for maintaining confidentiality of the data you will collect or will receive. Describe how you will protect the data from access by those not authorized. How will data be transmitted among research personnel? Where relevant, discuss the potential for deductive disclosure (i.e., directly identifying subjects from a combination of indirect IDs).

Personal identifying information obtained on the first two pages of the DCHS questionnaire and will be detached from the information related to the remainder of the questionnaire in accordance with Federal Privacy Act regulations. Recruitment lists with names and telephone numbers collected and stored in accordance with Federal Privacy Act regulations. Consent and assent forms administered for MICA study containing names that will be collected during the clinic visit will be stored in accordance with Federal Privacy Act regulations. All other forms and samples will have code numbers only and will be stored in a locked cabinet in a controlled Federal Facility.

A.4.11. **Data sharing.** With whom will *identifiable* (contains any of the 18 identifiers listed in question 9 above) data be shared outside the immediate research team? For each, explain confidentiality measures. Include data use agreements, if any.

X No one
__ Coordinating Center:
__ Statisticians:
__ Consultants:
__ Other researchers:
__ Registries:
__ Sponsors:
__ External labs for additional testing:
__ Journals:
__ Publicly available dataset:
__ Other:

A.4.12. **Data security for storage and transmission**. Please check all that apply.

For electronic data:

__X Secure network __ Password access __ Encryption
__ Other (describe):
__ Portable storage (e.g., laptop computer, flash drive)
Describe how data will be protected for any portable device:

For hardcopy data (including human biological specimens, CDs, tapes, etc.):

_X_ Data de-identified by research team (stripped of the 18 identifiers listed in question 7 above)
_X_ Locked suite or office
_X_ Locked cabinet
__ Data coded by research team with a master list secured and kept separately
__ Other (describe):

A.4.13. **Post-study disposition of identifiable data or human biological materials**. Describe your plans for disposition of data or human biological specimens that are identifiable in any way (directly or via indirect codes) once the study has ended. Describe your plan to destroy identifiers, if you will do so.

We do not expect any human biological materials to be left over. We are taking the minimal amount of biological samples in order to conduct the analyses.

Part A.5. The Consent Process and Consent Documentation (including Waivers)

The standard consent process is for all subjects to sign a document containing all the elements of informed consent, as specified in the federal regulations. Some or all of the elements of consent, including signatures, may be altered or waived under certain circumstances.

- If you will obtain consent in any manner, complete **section A.5.1**.
- If you are obtaining consent, but requesting a waiver of the requirement for a signed consent document, complete **section A.5.2**.
- If you are requesting a waiver of any or all of the elements of consent, complete **section A.5.3**.

You may need to complete more than one section. For example, if you are conducting a phone survey with verbal consent, complete sections A.5.1, A.5.2, and possibly A.5.3.

A.5.1. **Describe the process of obtaining informed consent from subjects**. If children will be enrolled as subjects, describe the provisions for obtaining parental permission and assent of the child. If decisionally impaired adults are to be enrolled, describe the provision for obtaining surrogate consent from a legally authorized representative (LAR). If non-English speaking people will be enrolled, explain how consent in the native language will be obtained. Address both written translation of the consent and the availability of oral interpretation. *After you have completed this part A.5.1, if you are not requesting a waiver of any type, you are done with Part A.5.; proceed to Part B.*

Parental Informed Consent:

As part of DCHS (EPA-05-144), the parents/guardians of up to 6,000 children will have received a written questionnaire. On the face-page of that questionnaire, the parents/guardians are informed that about 1,400 of the respondents might be re-contacted regarding a future clinical study. Parents or guardians who do not complete a questionnaire or communicate their refusal to participate will not be re-contacted for the clinical study.

Adult guardian/parents and children selected to participate in the MICA clinical study (see telephone script) will sign consent and assent forms respectively following a viewing of an on-site computer-based audiovisual presentation to include a basic educational module and visual/audio describing what will happen at each of the clinical stations.

Questionnaire:

A short respiratory health questionnaire administered at the day of the participant clinic visit will be used to gain insight into recent (1-week) health information, including dietary and environmental exposure data (attached). A poster with common asthma medications will be shown in the event that the participants fail to remember or record their medication type and dosage (attached). Each parent will complete the questionnaire with a provided #2 lead pencil. The front cover identifying the participant will be removed and filed separately. An identifying code will be attached to each of page of the questionnaire.

A.5.2. **Justification for a waiver of *written* (i.e., signed) consent**. *The default is for subjects to sign a written document that contains all the elements of informed consent.* Under limited circumstances, the requirement for a signed consent form may be waived by the IRB if either of the following is true: NA

a. The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality (e.g., study involves sensitive data that could be damaging if disclosed). __ yes __ no

Explain.

b. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context (e.g., phone survey). __ yes __ no

Explain.

If you checked "yes" to either, will consent be oral? Will you give out a fact sheet? Use an online consent form, or include information as part of the survey itself, etc?

If you have justified a waiver of written (signed) consent (A.5.2), you should complete A.5.3 *only* if your consent process will not include all the other elements of consent NA

3. **Justification for a full or partial waiver of consent.** *The default is for subjects to give informed consent.* A waiver might be requested for research involving only existing data or human biological specimens (see also Part C). More rarely, it might be requested when the research design requires withholding some study details at the outset (e.g., behavioral research involving deception). In limited circumstances, parental permission may be waived. This section should also be completed for a waiver of HIPAA authorization if research involves Protected Health Information (PHI) subject to HIPAA regulation, such as patient records.

__ Requesting **waiver of some elements** (specify; see SOP 28 on the IRB web site):
__ Requesting **waiver of consent entirely**
If you check either of the boxes above, answer items a-f.. To justify a full waiver of the requirement for informed consent, you must be able to answer "yes" (or "not applicable" for question c) to items a-f. **Insert brief explanations that support your answers.**

a. Will the research involve no greater than minimal risk to subjects or to their privacy? __ yes __ no
Explain.

b. Is it true that the waiver will *not* adversely affect the rights and welfare of subjects? *(Consider the right of privacy and possible risk of breach of confidentiality in light of the information you wish to gather.)* __ yes __ no
Explain.

c. When applicable to your study, do you have plans to provide subjects with pertinent information after their participation is over? *(e.g., Will you provide details withheld during consent, or tell subjects if you found information with direct clinical relevance? This may be an uncommon scenario.)* __ yes __ not applicable
Explain.

d. Would the research be impracticable without the waiver? *(If you checked "yes," explain how the requirement to obtain consent would make the research impracticable, e.g., are most of the subjects lost to follow-up or deceased?).* __ yes __ no
Explain.

e. Is the risk to privacy reasonable in relation to benefits to be gained or the importance of the knowledge to be gained? __ yes __ no
Explain.

If you are accessing patient records for this research, you must also be able to answer "yes" to item f to justify a waiver of HIPAA authorization from the subjects.

f. Would the research be impracticable if you could not record (or use) Protected Health Information (PHI)? *(If you checked "yes," explain how* not *recording or* __ yes __ no

using PHI would make the research impracticable).
Explain.

Part B. Questions for Studies that Involve Direct Interaction with Human Subjects

→ *If this does not apply to your study, do not submit this section.*

B.1. **Methods of recruiting.** Describe how and where subjects will be identified and recruited. Indicate who will do the recruiting, and tell how subjects will be contacted. Describe efforts to ensure equal access to participation among women and minorities. Describe how you will protect the privacy of potential subjects during recruitment. *For prospective subjects whose status (e.g., as patient or client), condition, or contact information is not publicly available (e.g., from a phone book or public web site), the initial contact should be made with legitimate knowledge of the subjects' circumstances. Ideally, the individual with such knowledge should seek prospective subjects' permission to release names to the PI for recruitment. Alternatively, the knowledgeable individual could provide information about the study, including contact information for the investigator, so that interested prospective subjects can contact the investigator.* Provide the IRB with a copy of any document or script that will be used to obtain the patients' permission for release of names or to introduce the study. Check with your IRB for further guidance.

As part of the DCHS (05-EPA-144), the Henry Ford Health System will identify two study populations from existing clinical records (a) 6000 children aged 7-12 who constitute a random sample of their client population (b) MICA subjects 100 asthmatic and 100 non-asthmatic children aged 9 to 12 years with a prior physician asthma diagnosis. Only those subjects whose parents returned the DCHS questionnaire packet will be eligible for MICA recruitment. Recruitment of asthmatics will be based on asthma emergency department visits and/or number of medication dispensing events. MICA subject recruitment will be limited to those parents who returned the DCHS questionnaire. See attached telephone script.

B.2. **Protected Health Information (PHI).** If you need to access Protected Health Information (PHI) to identify potential subjects who will then be contacted, you will need a *limited waiver of HIPAA authorization*. If this applies to your study, please provide the following information.

a. Will the information collected be limited only to that necessary to contact the subjects to ask if they are interested in participating in the study? NA

b. How will confidentiality/privacy be protected prior to ascertaining desire to participate? NA

c. When and how will you destroy the contact information if an individual declines participation? NA

B.3. **Duration of entire study and duration of an individual subject's participation, including follow-up evaluation if applicable.** Include the number of required contacts and approximate duration of each contact.

The study will be conducted in two phases during the 2006 calendar year. The IRB approved (EPA-05-144) questionnaire is scheduled for distribution during the late spring of 2006, before the end of the school year. The clinical measurements of exhaled breath and lung function, blood, urine and fingernail clipping collections will be scheduled for the summer and fall of

2006. Based on previous experience, we anticipate that the MICA clinical examinations will take the children up to 2 hours to complete. It has been estimated that MICA recruitment including clinical visits for 200 children will take approximately 8 weeks.

B.4. **Where will the subjects be studied?** Describe locations where subjects will be studied, both on and off the UNC-CH campus.

The clinical measurements of lung function and expired nitric oxide and the blood, urine and fingernail collections will be conducted in a clinical setting at the Henry Ford Health System's facilities in Detroit and Dearborn, MI. Families agreeing to the in home monitoring will be sent kits with detailed instructions. The monitors will be placed indoors and outdoors.

B.5. **Privacy.** Describe procedures that will ensure privacy of the subjects in this study. Examples include the setting for interviews, phone conversations, or physical examinations; communication methods or mailed materials (e.g., mailings should not indicate disease status or focus of study on the envelope).

All personal identifying information will be obtained on the first two pages of the approved DCHS questionnaire and the first page of the shorter day-of-clinic questionnaire (see questionnaire). These pages will be detached from the statistical information in the remainder of the questionnaire in accordance with Federal Privacy Act regulations. All personal identifying information will be stored in a separate locked filing cabinet in a controlled Federal facility.

B.6. **Inducements for participation.** Describe all inducements to participate, monetary or non-monetary. If monetary, specify the amount and schedule for payments and how this will be prorated if the subject withdraws (or is withdrawn) from the study prior to completing it. For compensation in foreign currency, provide a US$ equivalent. Provide evidence that the amount is not coercive (e.g., describe purchasing power for foreign countries). Include food or refreshments that may be provided.

Compensation for Clinic Samples

Compensation

Clinic Samples

Sample	Monetary Compensation	Notes
Blood, urine, fingernail (or toenail) clippings, odor identification test.	$65.00	See comment below
Lung function measurements (2)	$75.00	
	Total	
	$140.00	

Following the blood draw, the child will receive a small gift. If two attempts are made to obtain the blood and your child then provides urine, nail clippings and perform the odor identification test, you will receive $65. If after giving assent for the blood draw, your child refuses to have the

blood sample taken, we will not ask the child to provide urine, fingernails (or toenail) clippings, or to do the odor identification test, and no monetary compensation will be given for these tests. Whether or not they provide blood, your child will be asked to continue with the lung function measurements for which you could then receive $75.

Parents of children providing all clinic samples will receive a total of $140. However, only $75 will be provided to you at the end of the clinic visit. A check for the additional money will be mailed to you.

Home Samples

Sample	**Monetary Compensation**	**Notes**
Vacuum dust bag	$25.00	
Asthma/allergy medications	$10.00	
Indoor/outdoor passive samplers	$50.00	See comment below
	Total	
	$85.00	

Parents and children providing a list of asthma/allergy medications, home dust and air monitoring samples will receive up to an additional $85.00.

Comment: A select group of families were asked if they would be willing to have passive air samplers inside and outside their homes. If you volunteered to do the additional air sampling and are returning your sampling kit today, you would qualify for compensation noted above.

A duffle bag will be provided to all families that conduct air sampling to facilitate the return of the air sampling equipment. Families will be allowed to keep the duffle bag after they return the sampling equipment to the study.

Water will be offered at the start of the assent/consent process the day of the clinic visit.

B.7. **Costs to be borne by subjects.** Include child care, travel, parking, clinic fees, diagnostic and laboratory studies, drugs, devices, all professional fees, etc. If there are no costs to subjects other than their time to participate, indicate this.

Free parking is available at the Henry Ford Health Care System. For those people with no access to public transportation the cost of a taxi will be reimbursable. There are no study costs borne by the study subjects.